DATA EVALUATION RECORD - SUPPLEMENT

XDE-570 (FLORASULAM)

Study Type: Non-guideline; Preliminary Developmental Toxicity Study in Rats

Work Assignment No. 4-1-128 L (MRID 46808231)

Prepared for
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DATA EVALUATION RECORD

STUDY TYPE: Preliminary Prenatal Developmental Toxicity Study - Rats; Non-guideline

PC CODE: 129108 **DP BARCODE:** D331116
TXR#: 0054348

TEST MATERIAL (PURITY): XDE-570 (99.3% a.i.)

SYNONYMS: Florasulam; *N*-(2,6-Difluorophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo (1,5-*c*)pyrimidine-2-sulfonamide; XR-570; XRD-570; DE-570

CITATION: Liberacki, A. B, Breslin, W. J., and K. E. Stebbins (1996) XDE-570: oral gavage teratology probe study CD rats. The Toxicology Research Laboratory, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI. Laboratory Project Study ID: DR-0312-6565-024, June 12, 1996. MRID 46808231. Unpublished.

SPONSOR: DowElanco, 9330 Zionsville Road, Indianapolis, IN

EXECUTIVE SUMMARY: In a preliminary developmental toxicity study (MRID 46808231), XDE-570 (Florasulam; 99.3% a.i.; Lot No. 940714) in aqueous 0.5% methylcellulose was administered daily via oral gavage to ten time-mated CD rats/group at a dose volume of 4 mL/kg at dose levels of 0, 100, 500, or 1000 mg/kg/day from gestation day (GD) 6-15. Excessive maternal toxicity was observed in the 1000 mg/kg/day group, so two additional groups of ten rats were administered the test compound as previously described at dose levels of 0 or 750 mg/kg/day in order to more accurately determine the maximum tolerated dose. On GD 16, all surviving does were killed and a detailed necropsy was performed. The kidneys were removed and weighed, and the uterus and ovaries were removed and examined grossly for numbers of implantations, resorptions, and corpora lutea. Fetuses were not examined.

Five 1000 mg/kg/day dams were found dead on GD 10 (3 rats) and 13 (2 rats). Prior to death, two of these dams were observed with excessive chromorhinorrhea; and one also displayed decreased activity. Additionally at this dose, body weights were decreased ($p<=0.05$) by 7-8% on GD 9-12, resulting in a body weight loss on GD 6-9 (-3.8 g vs. 13.9 g in controls; $p<=0.05$) and decreased ($p<=0.05$) body weight gains on GD 9-12 (decr. 36%). Food consumption was also decreased (not significant [NS]) by 27% on GD 6-12. For these reasons, the surviving animals in this dose group were killed on GD 13 for humane reasons. No further data were collected or reported for this dose group.

In the remaining groups, no treatment-related effects were observed on mortality, clinical signs, or body weights. Gross pathology results were not provided for the 750 mg/kg/day group.

One 750 mg/kg/day dam was found dead on GD 15. This animal had no prior clinical signs of toxicity. At necropsy, this animal presented with decreased amounts of body fat, perineal soiling, hemolyzed blood in the digestive tract, erosions and/or ulcers in the stomach, and an enlarged spleen. The cause of death was attributed to a probable lymphoreticular tumor and uterine hemorrhage and was not considered treatment-related.

At 750 mg/kg/day, overall (GD 6-16) body weight gains were decreased (NS) by 14%, and food consumption was decreased by 5-10% during the treatment period. Additionally, absolute and relative (to body weight) kidney weights were increased ($p<=0.05$) by 12 and 16%, respectively.

The maternal LOAEL is 750 mg/kg/day, based on decreased body weight gains and food consumption, and increased kidney weights. The maternal NOAEL is 500 mg/kg/day.

There were no effects of treatment on the numbers of implantations, litters, or resorptions, or post-implantation losses. Fetal evaluations were not conducted.

The developmental LOAEL and NOAEL are not determined.

This study is classified **acceptable/non-guideline**.

COMPLIANCE: Signed and dated GLP Compliance, Quality Assurance, and Data Confidentiality statements were provided.

NOTE: This DER summarizes EPA conclusions regarding effects observed in the preliminary developmental toxicity study in rats. The summary was prepared from the original study; a full DER is not available.